REMARKS

In reply to the Office Action dated April 1, 2005, claims 35, 37, 63-69, and 104-109 are currently under examination in the Application. By the above amendment, claims 1-34, 36, 38-62, and 70-103 have been canceled and claims 63, 68, 69, and 109 have been amended solely to remove language directed to non-elected subject matter. Claims 104 and 106 have been amended to include recitation of "biodegradable". Support for the amendment can be found in the specification as filed, for example, on page 33, lines 1-13. No new matter has been added. The above amendment is not to be construed as acquiescence to the stated grounds for objection/rejection and is made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Applicants thank the Examiner for acknowledgement of the references submitted in the Information Disclosure Statements of July 10, 2003, and March 26, 2004.

Applicants also thank the Examiner for withdrawal of the previous rejections under 35 U.S.C. § 112.

Rejections under 35 U.S.C. § 112 (new matter)

Claims 104 and 106 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time the application was filed, had possession of the claimed invention. In particular, the Action contends that there is no support in the specification for the recitation of "microsphere" in that the specification allegedly only discloses the use of "biodegradable microspheres". The Action alleges that since the claim encompasses both nonbiodegradable and biodegradable, there is no written description of the scope of the claimed invention and the claimed invention constitutes new matter.

Without acquiescing to the rejection, Applicants have amended the claims to specifically recite "biodegradable microspheres". This amendment is made without prejudice to

prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Rejections under 35 U.S.C. § 112 (enablement)

Claims 35-37, 63-69, and 104-109 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Action contends that the breadth of the claimed invention is not enabled in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the *in vivo* treatment of disease in humans. The Action asserts that the state of the art is such that it is unpredictable whether the claimed method can be used *in vivo* in humans. In particular, the Action further alleges that the claimed method could not be used in most humans because they do not express an HLA allele which binds the peptide recited in the claims and that MHC binding alone is not evidence that peptide will actually generate a CTL response. The Action also cites the Ribi Adjuvant Systems fact sheet as evidence that the reagent is not for use in humans. Accordingly, the Action concludes that undue experimentation would be required to make and use the claimed invention.

Applicants traverse the rejection on the following grounds.

The thrust of the Action's assertions appears to be that the specification does not enable the use of the claimed methods due to a lack of evidence regarding their human implementation. If this is true, the Action is asserting that the claimed invention lacks *in vivo* utility. Although this rejection is not made under 35 U.S.C. § 101, the legal standard to be applied is the same. *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995) (Although the Examiner rejected the methods based on § 112, a § 101 rejection for lack of utility would also have been proper.) (See also "Legal Analysis Supporting Utility Examination Guidelines 60 F.R. 36263, July 14, 1995.)

Applicants respectfully submit that this rejection is improper in view of the PTO Guidelines. In *no* case has a Federal court required an applicant to support an asserted utility with data from human clinical trials. Moreover, in *In re Brana*, the Federal Circuit emphatically

rejected the PTO position that human clinical testing is necessary to establish practical utility for an antitumor agent. 51 F.3d 1560. Importantly, the court noted, citing *In re Krimmel*, 130 U.S.P.Q. 205 (C.C.P.A. 1961):

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, **even though it may eventually appear that the compound is without value in the treatment of humans**. (Emphasis added)

Here, the situation is analogous. Applicants have demonstrated in a mouse model a method of inducing an immune response using the recited WT1 peptide (see, in particular, Example 5); whether the method will eventually have commercial value in the treatment of humans is not a relevant inquiry to determine patentability.

In further support of the contention that the claims are not enabled, the Action contends that "tumor peptide vaccines are currently not used routinely in the treatment of human cancer". In this regard, Applicants note that to date there are dozens of clinical trials in the U.S., and many more around the world, that involve the use of tumor peptide vaccines for the treatment of cancer.

Concerning the Action's assertion that the claimed method could not be used in most humans because they do not express an HLA allele which binds the peptide recited in the claims, Applicants respectfully submit that, given the teachings of the specification, persons of ordinary skill in the art would readily be able to determine the appropriate setting for use of the claimed methods. Further, one skilled in the art would know how to determine the MHC type of a subject to be immunized. Even though the methods may not be operable in every human being, (*e.g.*, some embodiments may be inoperable), patentability is not precluded. The function of the claims is not to "specifically exclude...inoperative substances." (*Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984), citing *In re Dinh-Nguyen*, 492 F.2d 856 (CCPA 1974)).

With regard to the Action's contention that MHC binding alone is not evidence that peptide will actually generate a CTL response, Applicants note that the above remarks concerning inoperative embodiments apply equally herein. Further, Applicants respectfully note

that this is not relevant since the Applicants have clearly shown that the recited peptide set forth in SEQ ID NO:144 can induce an immune response *in vivo* (see Example 5).

Finally, concerning the Ribi Adjuvant Systems fact sheet cited by the Action, Applicants submit that the skilled artisan would readily appreciate that the "research use only-not for use in humans" proviso on the fact sheet provided by the Office is meant as a legal warning alerting customers to the licensed uses allowed, not as a scientific statement that the product **cannot** be used in humans. In fact, Applicants submit that MPL has been used in a variety of human clinical trials. According to the enclosed Vaccine Adjuvant information sheet, "MPL is now incorporated in two approved products and in multiple vaccines nearing approval around the world."

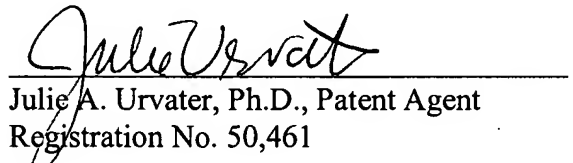
In view of the above remarks, Applicants submit that the claimed invention is enabled and respectfully request withdrawal of the rejection.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all the claims remaining in the application are now believed allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Vaccine Adjuvants

Corixa®

OVERVIEW

Corixa Corporation is one of the leading developers of vaccine adjuvants. Adjuvants are formulated compounds or additives that, when combined with vaccine antigens, help to direct or boost the body's immune system. Corixa's adjuvant technology stimulates the protective immune response that is normally initiated by the body during infection or injury. As a result of their increased potency, vaccines containing Corixa's adjuvants can produce greater vaccine protection within a shorter treatment time.

Corixa's flagship adjuvant, MPL®, is a derivative of the lipid A molecule. Found in gram-negative bacteria, lipid A is one of the most potent immune system stimulants. Together with its partners, Corixa is evaluating the use of MPL in vaccines targeting allergies, cancer and a variety of infectious diseases. Widely studied in the clinical setting, more than 273,000 doses of MPL adjuvant have been administered. In addition to MPL, Corixa has developed RC-529, a synthetic adjuvant with considerable potential for preventing and treating human diseases. RC-529 can produce both mucosal immunity (body surfaces) and systemic immunity (blood and internal organs). Furthermore, as a fully synthetic compound, RC-529 can be formulated for a variety of applications.

MARKET OPPORTUNITY

Adjuvants form the basis of Corixa's near-term commercialization strategy. The recent approval in Europe of Fendrix, GlaxoSmithKline's hepatitis B vaccine, which contains MPL, marks a significant commercialization milestone for Corixa's adjuvant business. MPL is now incorporated in two approved products and in multiple vaccines nearing approval around the world. Two other late-stage GSK vaccines that contain MPL include Simplirix, a vaccine for genital herpes, and Cervarix, a cervical cancer vaccine that targets the human papillomavirus. The markets for Simplirix and Cervarix are an estimated $850 million and $4 billion, respectively. Additional GSK vaccines containing MPL include a malaria vaccine, which recently completed a Phase IIb trial, as well as vaccines for tuberculosis prostate cancer and breast cancer. As part of its vaccine adjuvant license and supply agreements, Corixa stands to receive royalties on sales from all vaccines containing MPL.

ADJUVANT PRODUCT PIPELINE

Adjuvant	Product/Candidate	Disease Target	Development Phase	Partner
MPL	Fendrix vaccine	Hepatitis B in certain high-risk patients	Approved in E.U.	GlaxoSmithKline
RC-529	SUPERVAX vaccine	Hepatitis B	Approved in Argentina	Berna Biotech
MPL	Cervarix vaccine	Human papillomavirus	Phase III (two trials)	GlaxoSmithKline
MPL	Simplirix vaccine	Herpes simplex virus,	Phase III	GlaxoSmithKline
MPL	Pollinex Quattro vaccine	Allergies caused by grasses, trees, weeds and pollens	Phase III in E.U. — approved on named patient basis in Germany, Spain, Italy and U.K.	Allergy Therapeutics
MPL	Mosquirix vaccine	Malaria	Phase IIb trial in Mozambique	GlaxoSmithKline
MPL	BLP25 vaccine	Non-small cell lung cancer	Phase II	Biomira
MPL	Tuberculosis vaccine	Tuberculosis	Phase I	GlaxoSmithKline
MPL	Breast cancer vaccine	Breast cancer	Phase I	GlaxoSmithKline
MPL	Prostate cancer vaccine	Prostate cancer	Phase I	GlaxoSmithKline
RC-529	HepVax	Hepatitis B	IND application to be filed in 2005	Lorantis

RECENT ADJUVANT NEWS

Feb. 8, 2005 – GSK announces approval in Europe of Fendrix, GSK's hepatitis B vaccine, which contains MPL.

Oct. 14, 2004 – A proof-of-concept study of GSK's malaria vaccine, which contains MPL, is published in "The Lancet."

July 26, 2004 – Corixa enters new manufacturing and supply agreement with GSK, guaranteeing payment to Corixa for supplying GSK with increasing quantities of MPL.

March 30, 2004 – Corixa announces adjuvant license and supply agreements with Aventis Pasteur (Aventis). The agreement grants Aventis rights to Corixa's RC-529 adjuvant for use in multiple vaccines.

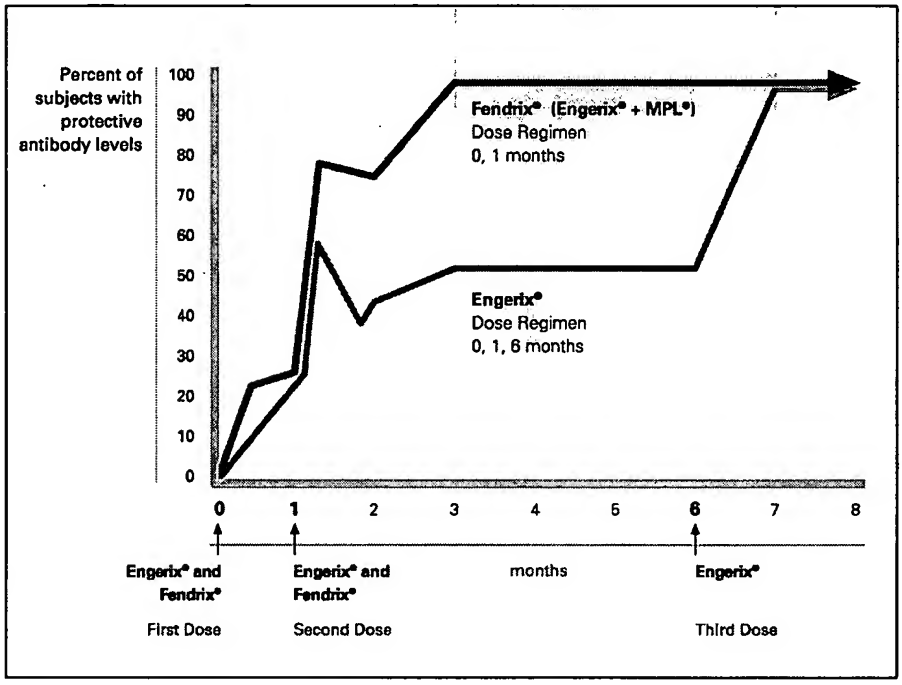
Vaccine Adjuvants

Corixa®

CLINICAL EXPERIENCE WITH MPL

In a GSK clinical trial involving nonresponders, Engerix-B, currently the world's leading hepatitis B vaccine, was compared with GSK's new vaccine, Fendrix, containing Corixa's MPL adjuvant. Investigators measured seroconversion rates (protective antibody levels) one month after each of three vaccine doses; at zero, one and six months. After the first dose, 78% of the group given the new vaccine seroconverted versus 59% of the Engerix-B. After two doses, 96% versus 76% seroconverted. After the third and final treatment, 98% of patients receiving Fendrix vaccine containing MPL adjuvant seroconverted compared to only 81% of patients given Engerix-B.

In a multi-center study of healthy individuals, more than 98% of those vaccinated with Fendrix achieved protective anti-hepatitis B antibody levels after just two doses, whereas three doses ofthe current Engerix-B product were required to obtain a similar level of protection.



GKS's Fendrix hepatitis B vaccine combines the antigen from Engerix-B with Corixa's MPL adjuvant. The resulting vaccine has an increased immune potency, allowing two dose administration rather than three.

TECHNICAL DESCRIPTION

MPL adjuvant is a proprietary form of monophosphoryl lipid A, a derivative of bacterial endotoxin, one of the most potent immune system stimulants known. Prepared from a heptoseless mutant of Salmonella minnesota, MPL is chemically similar to lipid A but lacks an acid-labile phosphoryl group and a base-labile acyl group. MPL retains the beneficial biological activities of lipid A but with a safety profile suitable for evaluation in pediatric applications.

MPL may be a key component of vaccines using technologies such as recombinant and synthetic antigens. While vaccines incorporating these antigens are considered safer than previous attenuated or killed whole-cell vaccines, many of them are poorly immunogenic in the absence of a potent adjuvant. MPL has demonstrated utility with peptide, bacterial sub-unit and synthetic polysaccharide antigens. Vaccines for infectious diseases and allergy desensitization containing this microbially derived adjuvant have demonstrated that MPL is well tolerated in human clinical trials involving thousands of doses.

MECHANISM OF ACTION

MPL activates cells of the monocyte/macrophage lineage and stimulates release of several cytokines, including IL-1, IL-12, TNFa and GM-CSF. Presumably through the action of these cytokines, lymphoid and antigen-presenting cells, including dendritic cells, are recruited to the local lymphoid organs where efficient immuno-enhancing cellular interactions can take place. These initial events mediated by MPL induce a strong TH1-type of cellular response characterized by increased production of IFN-g and IL-2. In turn, IFN-g promotes the production of complement fixing antibodies (i.e., IgG2a in the mouse), a hallmark of responses mediated by MPL.

MPL enhances immune responses to a variety of viral and bacterial antigen types, including peptides, proteins, polysaccharides and tumor cell lysates. Antigens successfully tested in preclinical studies include hepatitis B surface antigen, tetanus toxoid, trivalent split influenza, and a recombinant protein derived from the saliva-binding region of an adhesion protein of Streptococcus mutans. MPL produced striking results in studies with capsular polysaccharide antigens from organisms such as Hemophilus influenza b, several strains of pneumococcal bacteria and the Vi antigen from Salmonella typhi.